

Remarks

I. Status of the Claims

Claims 1-6 and 15-20 are pending in the application, with claim 1 being the sole independent claim.

II. Summary of the Office Action

In the final Office Action dated June 4, 2002, the Examiner has maintained one rejection of the claims. Applicant respectfully offers the following remarks to overcome or traverse this rejection.

III. The Rejection Under 35 U.S.C. § 102(e) Over the '365 Patent Is Traversed

In the Office Action at pages 2-3, the Examiner has maintained the rejection of claims 1-6 and 15-21 under 35 U.S.C. § 102(e) as being anticipated by Tabor *et al.*, U.S. Patent No. 5,614,365 (Doc. "A" cited on the Form PTO-892 attached to Paper No. 4; hereinafter "the '365 patent"). Applicant respectfully traverses this rejection, and reiterate and incorporates by reference herein the remarks concerning this same rejection that were provided in Applicant's Amendment and Reply Under 37 C.F.R. § 1.111 filed on December 4, 2001 (hereinafter "the 12/04/01 reply"). Applicant also wishes to provide the following additional remarks.

As noted in the 12/04/01 reply, the presently claimed invention has a date of invention that is prior to the earliest possible effective filing date of the '365 patent (*i.e.*, prior to October 17, 1994). Therefore, Applicant respectfully asserts that the '365 patent does not

qualify as a "patent granted on an application for patent by another filed in the United States before the invention" by the present Applicant. Hence, Applicant respectfully asserts that the '365 patent is not available as prior art against the presently claimed invention, and any rejection under 35 U.S.C. § 102 based on the disclosure of the '365 patent is in error. Reconsideration and withdrawal of the rejection therefore are respectfully requested.

Applicant notes that in making this rejection, the Examiner indicates that the Request for Interference Under 37 C.F.R. § 1.607, filed with the 12/04/01 reply, could not be located in the files of the USPTO. The Examiner further states that:

[u]ntil such time [as] a proper request for Interference under 37 CFR 1.607 is filed, [the] Examiner continues to maintain the above rejection.

Paper No. 12 at page 3, lines 11-12. During a telephone discussion with Applicant's undersigned representative on June 11, 2002, the Examiner stated that the remaining documents filed in support of the Rule 607 Request (viz., supporting declarations; Rule 608(b) Showing; etc.) were in the USPTO file, and that only the Rule 607 Request was missing. The Examiner also stated that if a copy of the Rule 607 Request filed on December 4, 2001, was provided with the present reply, then the document would be entered and considered.

Accordingly, attached hereto is a copy of the Request for Interference Under 37 C.F.R. § 1.607 that was filed in the present matter on December 4, 2001, along with a copy of the return receipt postcard bearing the date stamp evidencing receipt of this document by the USPTO on that date. As will be readily apparent upon review of this Request, the six requirements under 37 C.F.R. § 1.607 for a proper request for interference, which are identified by the Examiner in the Office Action at pages 2-3, are fulfilled by this Rule 607

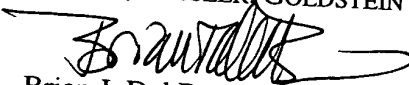
pleading. Applicant therefore respectfully requests that the Rule 607 Request for Interference be entered into the present application and that it be considered in view of the supporting documentation also previously provided. In light of the documents and evidence of record, Applicant also respectfully requests that the rejection under 35 U.S.C. § 102(e) be withdrawn and that an interference be expeditiously declared between the present application and U.S. Patent No. 5,614,365.

IV. Conclusion

All of the stated grounds of rejection have been properly traversed. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all of the outstanding rejections. It is believed that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.


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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Deb K. Chatterjee

Appln. No.: 09/558,421

Filed: April 26, 2000

For: **Mutant DNA Polymerases and
Uses Thereof**

Art Unit: 1652

Examiner: Rao, M.

Atty Docket: 0942.3600003/RWE/BJD

Request by Applicants for Interference Under 37 C.F.R. § 1.607

Commissioner for Patents
Washington, DC 20231

Sir:

Pursuant to the provisions of 37 C.F.R. § 1.607 and 1.643, Invitrogen Corporation, assignee of record of the entire interest of the present application,¹ requests the declaration of an interference between the present application (U.S. Appl. No. 09/558,421; hereinafter "the '421 application") and U.S. Patent No. 5,614,365 (hereinafter "the '365 patent"), to Tabor *et al.*, assigned to President & Fellow [sic; Fellows] of Harvard College, Cambridge, Massachusetts. The '365 patent is of record in the present case as Doc. No. A1 listed on the Form PTO-892 attached to Paper No. 4.

As noted in the cross-reference section of its specification, the above-captioned application is a continuation of U.S. Application No. 08/576,759, filed December 21, 1995,

¹ The present application was assigned by Deb K. Chatterjee to Life Technologies, Inc., in an Assignment recorded on December 21, 1995, at Reel 7842, Frame 0273. Life Technologies, Inc. merged with Invitrogen Corporation on September 12, 2000, with Invitrogen Corporation being the surviving entity. A copy of the merger document, evidencing this merger, is being filed for recordation with the Assignment Branch of the USPTO concurrently herewith. Therefore, Invitrogen Corporation is the assignee of record of the entire interest of the present application.

which is a continuation of U.S. Application No. 08/537,397, filed October 2, 1995, which is a continuation-in-part of U.S. Application No. 08/525,057, filed September 8, 1995. The '365 patent issued from U.S. Application No. 08/337,615, filed November 10, 1994, which is a continuation-in-part of U.S. Application No. 08/324,437, filed October 17, 1994.

Both the '365 patent and the present application disclose and claim mutant DNA polymerases, and DNA encoding them, comprising a Tyr → Phe mutation at a position corresponding to Phe₅₇₀ of wild-type T5 polymerase. Since the '365 patent and this application contain at least one claim directed to the same patentable invention, as discussed below, Applicant respectfully requests that an interference be expeditiously declared between the present application and the '365 patent.

I. Identification of Patent

In accordance with 37 C.F.R. § 1.607(a)(1), the patent with which Applicant seeks to have an interference declared is U.S. Patent No. 5,614,365, which issued on March 25, 1997, to Tabor *et al.*, and which is assigned to President & Fellow [sic; Fellows] of Harvard College, Cambridge, Massachusetts.

II. Proposed Count

In accordance with 37 C.F.R. § 1.607(a)(2), the following count is proposed:

A DNA molecule comprising a coding sequence for a mutant protein, wherein said mutant protein is a mutant DNA polymerase selected from the group consisting of: *E. coli* DNA polymerase I, Klenow fragment of *E. coli* DNA polymerase I, *Streptococcus pneumoniae* polymerase, *Thermus aquaticus* polymerase, *Thermus flavus* polymerase, *Thermus thermophilus* polymerase, *Deinococcus radiodurans* polymerase, *Bacillus caldotenax* polymerase, *E. coli* bacteriophage T5

polymerase, mycobacteriophage L5 polymerase, *Thermatoga maritima* polymerase, and *E. coli* bacteriophage SP01 polymerase, and wherein said mutant DNA polymerase comprises a substitution of Tyr for Phe at a position in said polymerase corresponding to Phe₅₇₀ of wild-type T5 polymerase.

This proposed count, which relates to a DNA molecule encoding a mutant DNA polymerase, encompasses all patentable claims which correspond to the count.

III. Identification of Claims in Patent Corresponding to the Proposed Count

In accordance with 37 C.F.R. § 1.607(a)(3), Applicant hereby identifies claims 1, 5, 6, 11 and 32 in the '365 patent as being directed to the same patentable invention as the proposed count, and which should therefore be designated as corresponding to the proposed count.

A. Claim 1

Claim 1 of the '365 patent recites:

1. Modified gene encoding a modified Pol I-type DNA polymerase wherein said modified gene is modified to encode a tyrosine residue at an amino acid position corresponding to T7 DNA polymerase residue 526 or at an amino acid position corresponding to *E. coli* DNA polymerase residue 762 in its dNMP binding site to increase ability of said modified DNA polymerase to incorporate a dideoxynucleotide relative to a corresponding deoxynucleotide compared to the ability of a corresponding naturally-occurring unmodified DNA polymerase by at least 20-fold.

This claim is therefore directed to the same patentable invention as the count and as Applicant's claims 1 and 15, since it encompasses modified DNA polymerases of the Pol I family with specific mutations corresponding to those recited in the count. While claim 1 of the

'365 patent refers to Pol I type DNA polymerases and Applicant's claim 1 recites a Markush group of specific polymerases, there is overlap between the two groups of polymerases. The Pol I family of polymerases is described in the '365 patent at col. 7, lines 40-46. This family of polymerases includes *Streptococcus pneumoniae* polymerase I, *Thermus aquaticus* polymerase I, *Thermus flavus* DNA polymerase, T5 DNA polymerase, and bacteriophage Spo 1 DNA polymerase, as well as other polymerases. Each of these specifically enumerated polymerases is recited in the Markush group in Applicant's claim 1 and in the proposed count. In addition, *Thermus aquaticus* polymerase is specifically recited in Applicant's claim 15 and in the proposed count. Finally, "a substitution of Tyr for Phe at a position in said polymerase corresponding to Phe₅₇₀ of wild-type T5 polymerase" recited in the count and in Applicant's claim 1, and substitution of tyrosine for phenylalanine at position 667 in Taq polymerase as recited in Applicant's claim 15, corresponds to a tyrosine substitution at position 762 of *E. coli* Pol I (see specification of '421 application, at page 8, lines 18 and 25), and to a tyrosine substitution at position 526 of T7 DNA polymerase (see '365 patent at Figs. 3 and 4, and at col. 3, line 59, to col. 4, line 4). Therefore, claim 1 of the '365 patent should be designated as corresponding to the count.

B. Claim 5.

Claim 5 of the '365 patent is directed to:

5. The modified gene of claim 1 wherein said modified DNA polymerase is a thermostable enzyme.

This claim is therefore directed to the same patentable invention as the count and as Applicant's claim 1, since a number of the enzymes recited in the Markush group of the count

and Applicant's claim 1 are thermostable enzymes (e.g., *Thermus aquaticus* polymerase, *Thermus flavus* polymerase, *Thermus thermophilus* polymerase and *Thermatoga maritima* polymerase). Hence, claim 5 of the '365 patent should be designated as corresponding to the count.

C. Claim 6

Claim 6 of the '365 patent is directed to:

6. The modified gene of claim 5 wherein said thermostable enzyme is selected from the group consisting of DNA polymerase encoded by *Thermus aquaticus*, *Thermus thermophilus*, *Thermus flavus*, and *Bacillus sterothermophilus*.

This claim is therefore directed to the same patentable invention as the count and as Applicant's claim 1, since a number of the enzymes recited in the Markush group of the count and Applicant's claim 1 are also recited in claim 6 of the '365 patent (i.e., *Thermus aquaticus* polymerase, *Thermus flavus* polymerase and *Thermus thermophilus* polymerase. Hence, claim 6 of the '365 patent should be designated as corresponding to the count.

D. Claim 11

Claim 11 of the '365 patent recites:

11. Method for production of a modified Pol I-type DNA polymerase having an increased ability to incorporate a dideoxynucleotide relative to a corresponding deoxynucleotide compared to ability of a corresponding naturally-occurring unmodified DNA polymerase comprising steps of: providing a nucleic acid molecule encoding a DNA polymerase and mutagenizing said nucleic acid molecule to incorporate one or more base

changes in nucleotide base sequence at a region that encodes its dNMP binding site to encode a tyrosine residue at an amino acid position corresponding to T7 DNA polymerase residue 526 or at an amino acid position corresponding to *E. coli* DNA polymerase residue 762 in the dNMP binding site to alter ability of said polymerase encoded by said nucleic acid to incorporate a dideoxynucleotide by at least 20-fold.

This claim is therefore directed to the same patentable invention as the count and as Applicant's claims 6 and 20, for essentially the same reasons outlined above with respect to claim 1 of the '365 patent, which are reiterated and incorporated herein. Hence, claim 6 of the '365 patent should be designated as corresponding to the count.

E. Claim 32

Claim 32 of the '365 patent recites:

32. Recombinant nucleic acid encoding any of the DNA polymerases of claims 27 to 31.

Claims 27 and 28, from which claim 32 depends in part, recite:

27. A *Thermus aquaticus* DNA polymerase having a tyrosine at residue 667.

28. An *E. coli* DNA polymerase I having a tyrosine at residue 762.

Hence, claim 32 of the '365 patent encompasses a recombinant nucleic acid molecule encoding (a) a Taq DNA polymerase having a tyrosine residue substituted in place of the phenylalanine residue at position 667 in the wild-type Taq sequence; and (b) an *E. coli* Pol I DNA polymerase having a tyrosine residue substituted in place of the phenylalanine residue at

position 762 in the wild-type *E. coli* Pol I sequence. This claim therefore is directed to the same patentable invention as Applicant's claim 1 and the proposed count, since "a substitution of Tyr for Phe at a position in said polymerase corresponding to Phe₅₇₀ of wild-type T5 polymerase" as recited in the proposed count would correspond to a substitution of tyrosine for phenylalanine at residue 667 of Taq, and at position 762 of *E. coli* Pol I. See specification of '421 application at page 8, lines 18, 20 and 25.

Claim 29, from which claim 32 of the '365 patent also depends, recited: of each of the

29. Purified Pol I type DNA polymerase having a tyrosine residue at an amino acid position corresponding to *E. coli* DNA polymerase residue 762 in its dNMP binding site provided that said polymerase is not a T7-type DNA polymerase or a mitochondrial DNA polymerase.

By its dependence from claim 29, claim 32 of the '365 patent therefore is similar to claim 1 of the present application and to claim 1 of the '365 patent. This claim is therefore directed to the same patentable invention as the count and as Applicant's claims 1 and 15, for essentially the same reasons outlined above with respect to claim 1 of the '365 patent which are reiterated and incorporated herein. For at least this additional reason, then, claim 32 of the '365 patent should be designated as corresponding to the count.

IV. Identification of Claims in Present Application Corresponding to the Proposed Count

Upon entry of the Amendment and Reply Under 37 C.F.R. § 1.111 filed concurrently herewith, claims 1-6 and 15-20 are pending in the present application. In accordance with 37 C.F.R. § 1.607(a)(4), Applicant respectfully submits that each of the pending claims corresponds to the proposed count.

The proposed count, directed to a DNA molecule, is identical to claim 1 of the captioned application. This claim defines the same patentable invention as the count and should be designated as corresponding to the count.

Claim 2 of this application is dependent on claim 1 and relates to a DNA molecule of claim 1 further comprising a promoter. This claim defines the same patentable invention as the count and should be designated as corresponding to the count.

Claim 3 of this application is dependent on claim 2 and relates to a DNA molecule of claim 2, wherein the coding sequence is heterologous to the promoter. This claim defines the same patentable invention as the count and should be designated as corresponding to the count.

Claim 4 of this application relates to a host cell comprising the DNA molecule of claim 1. This claim defines the same patentable invention as the count and should be designated as corresponding to the count.

Claim 5 of this application is dependent on claim 4, and further defines the host cell to be *E. coli*. This claim defines the same patentable invention as the count and should be designated as corresponding to the count.

Claim 6 relates to a method of producing a mutant DNA polymerase by culturing a host cell comprising the DNA molecule of claim 2. This claim defines the same patentable invention as the count and should be designated as corresponding to the count.

Claims 15-20 relate to a DNA molecule comprising a coding sequence for a mutant *Taq* DNA polymerase comprising a substitution of Tyr for Phe₆₆₇ of wild-type *Taq* polymerase, a host cell comprising this DNA molecule, a method for producing a mutant DNA polymerase using this DNA molecule, and the mutant *Taq* DNA polymerase. Position 667 of *Taq* polymerase corresponds to position 570 of T5 polymerase (*see* Specification of the '421 application, at 8.)

These claims define the same patentable invention as the count and should be designated as corresponding to the count.

Consequently, Applicant submits that claims 1-6 and 15-20, which are all the claims that are pending in the present application, should be designated as corresponding to the count.

V. *Application of Claims 1-6 and 15-20 to the Disclosure of the '421 application*

In accordance with 37 C.F.R. § 1.607(a)(5), the terms of claims 1-6 and 15-20 of the present application, identified above as corresponding to the count, are supported in the present specification at least according to the following chart:

'421 Application Claims	'421 Application Disclosure
1. A DNA molecule comprising a coding sequence for a mutant protein, wherein said mutant protein is a mutant DNA polymerase . . .	"The invention also relates to a DNA molecule which codes for the mutant DNA polymerase of the present invention . . ." Page 4, lines 4-5

<p>selected from the group consisting of: <i>E. coli</i> DNA polymerase I, Klenow fragment of <i>E. coli</i> DNA polymerase I, <i>Streptococcus pneumoniae</i> polymerase, <i>Thermus aquaticus</i> polymerase, <i>Thermus flavus</i> polymerase, <i>Thermus thermophilus</i> polymerase, <i>Deinococcus radiodurans</i> polymerase, <i>Bacillus caldodenax</i> polymerase, <i>E. coli</i> bacteriophage T5 polymerase, mycobacteriophage L5 polymerase, <i>Thermatoga maritima</i> polymerase, and <i>E. coli</i> bacteriophage SP01 polymerase . . .</p>	<p>“ . . . it is also possible to prepare the following mutant DNA polymerases:</p> <table border="1"> <thead> <tr> <th>Enzyme or source Position</th><th>Mutation</th></tr> </thead> <tbody> <tr> <td><i>E. coli</i> DNA polymerase I</td><td>762</td></tr> <tr> <td><i>Streptococcus pneumoniae</i></td><td>711</td></tr> <tr> <td><i>Thermus aquaticus</i></td><td>667</td></tr> <tr> <td><i>Thermus flavus</i></td><td>666</td></tr> <tr> <td><i>Thermus thermophilus</i></td><td>669</td></tr> <tr> <td><i>Deinococcus radiodurans</i></td><td>747</td></tr> <tr> <td><i>Bacillus caldodenax</i></td><td>711</td></tr> <tr> <td><i>E. coli</i> bacteriophage T5</td><td>570</td></tr> <tr> <td>mycobacteriophage L5</td><td>438</td></tr> <tr> <td><i>E. coli</i> bacteriophage SP01</td><td>692</td></tr> <tr> <td><i>E. coli</i> bacteriophage SP02</td><td>447</td></tr> <tr> <td><i>Thermatoga neapolitana</i></td><td>67 []</td></tr> <tr> <td><i>Thermatoga maritima</i></td><td>730”</td></tr> </tbody> </table> <p>Page 8, lines 15-30.</p>	Enzyme or source Position	Mutation	<i>E. coli</i> DNA polymerase I	762	<i>Streptococcus pneumoniae</i>	711	<i>Thermus aquaticus</i>	667	<i>Thermus flavus</i>	666	<i>Thermus thermophilus</i>	669	<i>Deinococcus radiodurans</i>	747	<i>Bacillus caldodenax</i>	711	<i>E. coli</i> bacteriophage T5	570	mycobacteriophage L5	438	<i>E. coli</i> bacteriophage SP01	692	<i>E. coli</i> bacteriophage SP02	447	<i>Thermatoga neapolitana</i>	67 []	<i>Thermatoga maritima</i>	730”
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<p>wherein said mutant DNA polymerase comprises a substitution of Tyr for Phe at a position in said polymerase corresponding to Phe₅₇₀ of wild-type T5 polymerase.</p>	<p>“The change in amino acid at the mutation positions above is from phenylalanine to tyrosine . . .”</p> <p>Page 8, lines 31-32.</p>																												
<p>2. The DNA molecule of claim 1, further comprising a promoter, . . .</p>	<p>“the recombinant DNA molecule encodes the protein, and also includes a promoter. . .”</p> <p>Page 15, lines 7-8.</p>																												
<p>wherein said promoter is in a position and orientation with respect to the coding sequence such that the mutant protein may be expressed in a cell under the control of said promoter.</p>	<p>“(The promoter and the structural gene are in such position and orientation with respect to each other that the promoter may regulate the expression of the gene in the cell).”</p> <p>Page 15, lines 9-11.</p>																												

<p>3. The molecule of claim 2, wherein said coding sequence is heterologous to said promoter.</p>	<p>"The promoter may be heterologous to the structural gene and may be inducible, e.g. a <i>lambda</i> P_L promoter, a <i>tac</i> promoter, or a <i>lac</i> promoter. Preferably, the structural gene is under control of a heterologous promoter."</p> <p>Page 15, lines 15-17.</p>
<p>4. A host cell comprising the DNA molecule of claim 1.</p>	<p>"The invention also relates to a DNA molecule which codes for the mutant DNA polymerase of the present invention as well as host cells comprising the DNA molecule."</p> <p>Page 4, lines 4-6.</p>
<p>5. The host cell of claim 4, wherein said host cell is <i>E. coli</i>.</p>	<p>"Preferably, the mutant DNA polymerase gene is expressed and maintained in an <i>E. coli</i> host cell."</p> <p>Page 15, lines 13-14.</p>
<p>6. A method for producing a protein, wherein said protein is a mutant DNA polymerase . . .</p>	<p>"The invention also relates to a method for producing a protein, wherein said protein has a mutant DNA polymerase activity . . ."</p> <p>Page 4, lines 7-8.</p>

<p>selected from the group consisting of: <i>E. coli</i> DNA polymerase I, Klenow fragment of <i>E. coli</i> DNA polymerase I, <i>Streptococcus pneumoniae</i> polymerase, <i>Thermus aquaticus</i> polymerase, <i>Thermus flavus</i> polymerase, <i>Thermus thermophilus</i> polymerase, <i>Deinococcus radiodurans</i> polymerase, <i>Bacillus caldovenax</i> polymerase, <i>E. coli</i> bacteriophage T5 polymerase, mycobacteriophage L5 polymerase, <i>Thermatoga maritima</i> polymerase, and <i>E. coli</i> bacteriophage SP01 polymerase, . . .</p>	<p>“ . . it is also possible to prepare the following mutant DNA polymerases:</p> <table border="1"> <thead> <tr> <th>Enzyme or source</th><th>Mutation</th></tr> </thead> <tbody> <tr> <td><i>E. coli</i> DNA polymerase I</td><td>762</td></tr> <tr> <td><i>Streptococcus pneumoniae</i></td><td>711</td></tr> <tr> <td><i>Thermus aquaticus</i></td><td>667</td></tr> <tr> <td><i>Thermus flavus</i></td><td>666</td></tr> <tr> <td><i>Thermus thermophilus</i></td><td>669</td></tr> <tr> <td><i>Deinococcus radiodurans</i></td><td>747</td></tr> <tr> <td><i>Bacillus caldovenax</i></td><td>711</td></tr> <tr> <td><i>E. coli</i> bacteriophage T5</td><td>570</td></tr> <tr> <td>mycobacteriophage L5</td><td>438</td></tr> <tr> <td><i>E. coli</i> bacteriophage SP01</td><td>692</td></tr> <tr> <td><i>E. coli</i> bacteriophage SP02</td><td>447</td></tr> <tr> <td><i>Thermatoga neapolitana</i></td><td>67 []</td></tr> <tr> <td><i>Thermatoga maritima</i></td><td>730”</td></tr> </tbody> </table> <p>Page 8, lines 15-30.</p>	Enzyme or source	Mutation	<i>E. coli</i> DNA polymerase I	762	<i>Streptococcus pneumoniae</i>	711	<i>Thermus aquaticus</i>	667	<i>Thermus flavus</i>	666	<i>Thermus thermophilus</i>	669	<i>Deinococcus radiodurans</i>	747	<i>Bacillus caldovenax</i>	711	<i>E. coli</i> bacteriophage T5	570	mycobacteriophage L5	438	<i>E. coli</i> bacteriophage SP01	692	<i>E. coli</i> bacteriophage SP02	447	<i>Thermatoga neapolitana</i>	67 []	<i>Thermatoga maritima</i>	730”
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<p>comprising a substitution of Tyr for Phe at a position in said polymerase corresponding to Phe₅₇₀ of wild-type T5 polymerase, . . .</p>	<p>“The change in amino acid at the mutation positions above is from phenylalanine to tyrosine . . .”</p> <p>Page 8, lines 31-32.</p>																												
<p>said method comprising: (a) culturing a host cell comprising the DNA molecule of claim 2, and (b) isolating said protein from said host cell.</p>	<p>“said method comprising the steps of: (i) culturing a host cell containing the DNA molecule of the invention, and (ii) isolating said protein from said host cell.”</p> <p>Page 4, lines 9-13.</p>																												
<p>15. A DNA molecule as claimed in claim 1, wherein said mutant protein is a mutant Taq DNA polymerase comprising a substitution of Tyr for Phe₆₆₇ of wild-type Taq polymerase.</p>	<p>“Examples of such mutant DNA polymerase proteins include . . . mutant Taq DNA polymerase, wherein Tyr⁶⁶⁷ is substituted for Phe⁶⁶⁷ of native Taq DNA polymerase;”</p> <p>Page 4, lines 14 and 16-17.</p>																												

16. The DNA molecule of claim 15, further comprising a promoter, . . .	<p>"the recombinant DNA molecule encodes the protein, and also includes a promoter. . ."</p> <p>Page 15, lines 7-8.</p>
wherein said promoter is in a position and orientation with respect to the coding sequence such that the mutant protein may be expressed in a cell under the control of said promoter.	<p>"(The promoter and the structural gene are in such position and orientation with respect to each other that the promoter may regulate the expression of the gene in the cell)."</p> <p>Page 15, lines 9-11.</p>
17. The molecule of claim 16, wherein said coding sequence is heterologous to the promoter.	<p>"The promoter may be heterologous to the structural gene and may be inducible, e.g. a <i>lambda</i> P_L promoter, a <i>tac</i> promoter, or a <i>lac</i> promoter. Preferably, the structural gene is under control of a heterologous promoter."</p> <p>Page 15, lines 15-17.</p>
18. A host cell comprising the DNA molecule of claim 15.	<p>"The invention also relates to a DNA molecule which codes for the mutant DNA polymerase of the present invention as well as host cells comprising the DNA molecule."</p> <p>Page 4, lines 4-6.</p>
19. The host cell of claim 18, wherein said host cell is <i>E. coli</i> .	<p>"Preferably, the mutant DNA polymerase gene is expressed and maintained in an <i>E. coli</i> host cell."</p> <p>Page 15, lines 13-14.</p>

<p>20. A method for producing a protein, . . .</p>	<p>"The invention also relates to a method for producing a protein, wherein said protein has a mutant DNA polymerase activity . . ."</p> <p>Page 4, lines 7-8.</p>
<p>wherein said protein is a mutant Taq DNA polymerase comprising a substitution of Tyr for Phe₆₆₇ of wild-type Taq polymerase, . . .</p>	<p>"Examples of such mutant DNA polymerase proteins include . . . mutant Taq DNA polymerase, wherein Tyr⁶⁶⁷ is substituted for Phe⁶⁶⁷ of native Taq DNA polymerase;"</p> <p>Page 4, lines 14 and 16-17.</p>
<p>said method comprising: (a) culturing a host cell comprising the DNA molecule of claim 16, and (b) isolating said protein from said host cell.</p>	<p>"said method comprising the steps of: (i) culturing a host cell containing the DNA molecule of the invention, and (ii) isolating said protein from said host cell."</p> <p>Page 4, lines 9-13.</p>

VI. Compliance with 37 C.F.R. § 1.607(a)(6)

An Applicant seeking to provoke an interference with an issued patent must "[e]xplain[] how the requirements of 35 U.S.C. § 135(b) are met, if the claim presented or identified under paragraph (a)(4) of this section was not present in the application until more than one year after the issue date of the patent." 37 C.F.R. § 1.607(a)(6). The claims currently pending in the present application, and identified above under 37 C.F.R. § 1.607(a)(4) as corresponding to the proposed count, were filed in the present application on April 26, 2000. Moreover, the present application is a continuation of U.S. Application No. 08/576,759, filed December 21, 1995, which is a continuation of U.S. Application No. 08/537,397, filed October 2, 1995; both of these priority applications contained at least claims 1-6 and 15-20 as currently presented. Therefore, Applicant respectfully submits that these claims have been pending in the present application since at least

December 21, 1995, or since at least October 2, 1995, both of which predate the issue date of the '365 patent (March 25, 1997). Thus, the claims identified above under 37 C.F.R. § 1.607(a)(4) were present in the present application prior to the issue date of the '365 patent. Accordingly, it is respectfully believed that there is no requirement for an explanation under 37 C.F.R. § 1.607(a)(6) of how the requirements of 35 U.S.C. § 135(b) are met.

VII. *The '365 Patent Does Not Constitute Potential Prior Art under Section 102(e) in Light of the Showing Relating to Priority of Invention*

As discussed *supra*, Applicant has submitted evidence under 37 C.F.R. § 1.608(b) establishing conception and reduction to practice of his invention prior to the earliest available filing date of Tabor '437 (October 17, 1994). This conception and reduction to practice have been fully corroborated. Therefore, the '365 patent does not constitute prior art to the present application under 35 U.S.C. § 102(e), and it is respectfully believed that an interference between the present application and the '365 patent may be properly declared. *See* MPEP § 2306 (August 2001).

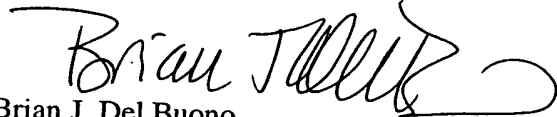
VIII. *Summary*

In light of the foregoing, and of the attached evidence and remarks contained in Applicant's Amendment and Reply Under 37 C.F.R. § 1.111 and in the Showing Under 37 C.F.R. § 1.608(b) filed concurrently herewith, Applicant respectfully requests that an interference be expeditiously declared between the present application and U.S. Patent No. 5,614,365. Early notification to this effect is earnestly solicited.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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Applicant: Chatterjee, D.K.

Due Date: December 4, 2001

Application No.: 09/558,421

Art Unit: 1652

Filed: April 26, 2000

Examiner: Rao, M.

For: Mutant DNA Polymerases and Uses Thereof

Docket: 0942.3600003

Atty: RWE/BJD

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

- 1) SKGF Cover Letter (*in duplicate*); 2) PTO Fee Transmittal Form (PTO/SB/17) (*in duplicate*); 3) Our check in the amount of \$920.00 to cover the appropriate fee for a three-month extension of time; 4) Petition For Extension of Time Under 37 C.F.R. § 1.136(a)(1) (*in duplicate*); 5) Amendment and Reply Under 37 C.F.R. § 1.111; 6) Request by Applicants for Interference Under 37 C.F.R. § 1.607; 7) Showing Under 37 C.F.R. § 1.608(b) including copies of the Declaration of Harini Shandilya with attached Exhibits A-D, the Declaration of Flora Lichaa with attached Exhibit A, and the Declaration of Gary Gerard with attached Exhibits A-C; 8) Declaration of Deb. K. Chatterjee Under 37 C.F.R. § 1.131(a) with attached Exhibits A through J, C-1 through C-15, F-1 through F-18, G-1, G-2, H-1, K-1 through K-37, L-1 through L-176, M-1 through M-6, P-1 through P-13, and S-1 through S-7; 9) Declaration of Roger Lasken with attached Exhibits A, and 1 through 175; 10) Declaration of Elizabeth Flynn with attached Exhibits A, and 1 through 18; 11) Declaration of Adam Goldstein with attached Exhibits A, and 1 through 3; 12) Declaration of A. John Hughes, Jr. with attached Exhibits A, and 1; 13) Declaration of Mary Longo with attached Exhibits A, and 1 through 7; 14) Declaration of Brian Schmidt with attached Exhibits A, and 1 through 20; 15) Declaration of Kalavathy Sitaraman with attached Exhibits A, and 1 through 37; and 16) One (1) return postcard.

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